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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/927,914 | 08/10/2001 | Timothy P. Tully | 1314.2004-001 | 5180 |

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| EXAMINER | |
|---|---|
| CHONG, YONG SOO | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/927,914 | TULLY ET AL. | |
| | Examiner | Art Unit | |
| | YONG S. CHONG | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,4-10,12-14,16-22,24-49,51-57,59-93,98 and 100-104* is/are pending in the application.

4a) Of the above claim(s) *2,9,10,12,13,21,22,24-48,59 and 65-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98, 100-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/08, 5/22/08*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Application*

This Office Action is in response to applicant's arguments filed on 5/6/08. Claims 3, 11, 15, 23, 50, 58, 94-97, 99, 105-106 have been cancelled. Claims 1-2, 4-10, 12-14, 16-22, 24-49, 51-57, 59-93, 98, 100-104 are pending. Claims 1, 5, 8, 14, 17, 20, 49, 53, 56-57, 61, 64, 98, 101, 104 have been amended. Claims 2, 9-10, 12-13, 21-22, 24-48, 59, 65-93 have been withdrawn. Claims 1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98, 100-104 are examined herein.

Applicant's amendments to the claims have rendered the 112 rejection of the last Office Action moot, therefore hereby withdrawn.

Applicant's arguments have been fully considered but found not persuasive. The 103(a) rejection of the last Office Action is maintained for reasons of record and modified below as a result of Applicant's amendment to the claims.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-8, 14, 16-20, 49, 51-57, 60-64, 98, 100-104 are rejected under 35 U.S.C. 103(a) as being obvious over Christensen et al. (US Patent 5,547,979) in view of the Merck Manual (of record).

The instant claims are directed to a method of increasing performance gain during treatment of a cognitive deficit associated with a central nervous system disorder by providing cognitive training and administering a phosphodiesterase 4 inhibitor.

Christensen et al. teach the phosphodiesterase inhibitor, rolipram (col. 11, line 14), in a method of treating stroke in a human (claim 1). The active ingredient may be administered from 1 to 6 times a day (col. 8, lines 62-64) or as recognized by one of ordinary skill in the art that the optimal quantity and spacing of individual dosages will be determined by the nature and extent of the condition, the form, route, site of administration, patient, and that such optimums can be determined by conventional techniques (col. 10, lines 29-41).

It is noted that the limitations regarding “which enhances CREB pathway function” and “wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain” are given little patentable weight, because these

biological processes are inherent when the same compound is administered in the same patient population at the same dosage.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

However, Christensen et al. fail to disclose multiple cognitive training sessions sufficient to produce an improvement in performance of a cognitive task whose deficit is associated with a central nervous system disorder.

The Merck Manual teaches that a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises, if possible, should be started early (pg. 1455-1456). It is noted that these rehabilitation techniques meet the limitation of cognitive training. Furthermore, it is obvious to one of ordinary skill in the art to not stop at a single training session in the rehabilitation of a stroke victim since the process takes a great deal of time with many repeated sessions.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of treating stroke in a human, as disclosed by Christensen et al.

A person of ordinary skill in the art would have been motivated to combine the two disclosed methods of treating a stroke patient because: (1) both Christensen and the Merck Manual disclose treatment for the same purpose, which is treating stroke patients and because (2) of the additive therapeutic effects of employing two methods of treating stroke simultaneously. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating stroke in a human by administering a phosphodiesterase inhibitor, rolipram, in conjunction with a cognitive training protocol, outlined by the Merck Manual.

***Response to Arguments***

Applicant argues that Christensen relates to administration of rolipram during the initial acute phase of a stroke episode to treat acute tissue injury. Christensen does not teach or suggest that the compounds are phosphodiesterase inhibitors. Christensen does not teach the administration of the compounds after the acute phase of the inflammatory event has ended or during training. Christensen along with the Merck Manual does not teach that one could achieve performance gain during the training by the administration of phosphodiesterase inhibitors before or during training.

This is not persuasive because, at the outset, it is confusing why Applicant continues to argue that Christensen does not teach phosphodiesterase inhibitor when even Applicant admits on the record that rolipram is taught. This is the same exact compound that is in Applicant's specification that is disclosed to be a phosphodiesterase 4 inhibitor. Is it because it is not specifically disclosed to be a phosphodiesterase 4 inhibitor by Christensen? If that is the case, it is Applicant's burden to show through factual data that the rolipram in Christensen does not work in the same manner as the rolipram in the instant invention.

Furthermore, it is not certain why Christensen must teach the administration of phosphodiesterase inhibitors after the acute phase of the inflammatory event has ended or during training. The reason why this is confusing is because the instant claims recite administration of phosphodiesterase inhibitors before, during, or after cognitive training, which means administration at any time during the treatment period. Applicant is clearly trying to distance themselves from the teachings of cited prior art by importing limitations into the claims, which are not present. At any rate, the cited prior art still reads on the instant claims. Examiner reminds Applicant that Christensen clearly discloses the claimed phosphodiesterase inhibitor and that the Merck Manual discloses cognitive training, both references for the purpose of treating stroke victims.

Applicant argues hindsight reconstruction in the argument that performance gain would necessarily result if rolipram therapy is administered immediately following stoke and cognitive therapy is begun as early as possible after stroke. Applicant argues that the Examiner has provided no evidence that the administration timeline contemplated

by Christensen overlaps with that described by the Merck Manual. Specifically, Applicant argues that neither of the cited references teach or suggest "long-lasting performance gain effected by enhancement of CREB pathway function during rehabilitation."

This is not persuasive because said performance gain of a cognitive task in a stroke patient is an inherent property when the same compound is administered to the same patient at the same dose. Therefore, the "long lasting" and "enhancement of CREB pathway function" limitations are met because they are inherent properties. Moreover, the Examiner interprets performance gain of a cognitive task as covering a wide range of impairments, which include aphasia (language/speech disturbance) and apraxia (impaired ability to carry out motor activities), as disclosed in Applicant's own disclosure. Essentially, the scope of the instant claims covers administration of the phosphodiesterase inhibitors at any time to the patient. Therefore, Applicant's assertion that Christensen is simply teaching the administration of rolipram during the acute phase of the stroke to reduce TNF still meets the limitations of the instant claims as it relates to the Merck Manual reference. Nonetheless, Applicant is invited to show factual data that performance gain would not result in the method taught by the cited prior art references.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's arguments directed to the new limitation of "repeated administration of steps (a) and (b)" have been addressed in the modified rejection above.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S Chong/
Examiner, Art Unit 1617

YSC